

**WHAT IS CLAIMED IS:**

1. A stabilizing catheter for protein drug delivery to a user, the stabilizing catheter comprising:
  - a tubing including at least one layer, wherein the at least one layer includes one or more materials that reduce diffusion of small molecules through the tubing, such that when the tubing is used for protein drug delivery, the protein drug formulation is maintained as compared with the protein drug formulation delivered via a different tubing including one or more materials that are free of an effect that reduces diffusion of small molecules through the tubing.
2. The stabilizing catheter of claim 1, wherein an insulin formulation is maintained in the tubing to substantially prevent occlusions or deposits from being formed during insulin delivery.
3. The stabilizing catheter of claim 1, wherein an insulin formulation is stabilized by being substantially free of deposits or occlusions comprising insulin and an excipient.
4. The stabilizing catheter of claim 2, wherein the insulin is a high concentration formulation.
5. The stabilizing catheter of claim 4, wherein the high concentration formulation is greater than about 100U/ml.

- 25 6. The stabilizing catheter of claim 1, wherein the one or more materials of the at least one layer includes materials selected from at least polytetrafluoroethane, saran (PVOC) polysulfone, glass, metal, derivatives of these materials, and mixtures of these materials.

7. The stabilizing catheter of claim 6, wherein the glass includes glass fibers.

8. The stabilizing catheter of claim 6, wherein the metal includes a braided metal.

5 9. The stabilizing catheter of claim 9, wherein the tubing includes at least two layers.

10 10. The stabilizing catheter of claim 9, wherein one layer includes materials selected from at least polytetrafluoroethane, saran (PVOC), polysulfide, glass, metal, derivatives of these materials, and mixtures of these materials.

10 11. The stabilizing catheter of claim 9, wherein one layer includes silicone, polyurethane, derivatives of these materials or mixtures of these materials.

15 12. The stabilizing catheter of claim 12, wherein the layer including silicone, polyurethane, derivatives of these materials or mixtures of these materials is the outer layer of the tubing.

13. The stabilizing catheter of claim 9, comprising an innermost layer that is formed from one or more hydrophilic protein compatible materials.

20 14. The stabilizing catheter of claim 13, wherein the hydrophilic protein compatible materials are selected from at least a polyethylene glycol, a polyurethane, a Genapol, a Tween, a Triton-X and a Brij, derivatives of these materials and mixtures of these materials.

15. The stabilizing catheter of claim 9, comprising three layers, an outer layer including a silicone material and a layer including materials selected from at least polytetrafluoroethane, saran (PVOC), polysulfone, glass, metal, derivatives of these materials, and mixtures of these materials, and an innermost layer that includes one or more hydrophilic 5 insulin compatible materials.

16. The stabilizing catheter of claim 1, wherein the small molecules have a molecular weight of about 18 g/mole to about 500 g/mole.

10 17. The stabilizing catheter of claim 1, wherein the small molecules include neutral molecules, charged molecules, or mixtures of these molecules.

15 18. The stabilizing catheter of claim 17, wherein the charged molecules include metal ions.

19. The stabilizing catheter of claim 17, wherein the neutral molecules include at least phenol, phenolic derivatives, carbon dioxide, or mixtures of these molecules.

20 20. The stabilizing catheter of claim 19, wherein the stabilizing catheter reduces a diffusional flow of carbon dioxide into the tubing up to about 1000 fold as compared to the diffusional flow of carbon dioxide into a different tubing that is free of a stabilizing layer.

25 21. The stabilizing catheter of claim 20, wherein the stabilizing catheter reduces a diffusional flow of carbon dioxide into the tubing about 10-100 fold.

22. The stabilizing catheter of claim 19, wherein the stabilizing catheter reduces a diffusional flow of phenol, phenolic derivatives, or both, out from the tubing up to about 100

fold as compared to the diffusional flow of phenol, phenolic derivatives, or both, out from a different tubing that is free of a stabilizing layer.

5        23.      The stabilizing catheter of claim 22, wherein the stabilizing catheter reduces a diffusional flow of carbon dioxide into the tubing about 2-20 fold.

10       24.      The stabilizing catheter of claim 19, wherein the stabilizing catheter provides a diffusional barrier to phenol and phenolic derivatives such that the loss of phenol and phenolic derivatives through the tubing is less than about 5%, +/- 1%, at an protein drug infusion rate of about 20 U/day.

15       25.      The stabilizing catheter of claim 6, where the layer of Teflon and/or saran is about 0.002 in to about 0.02 in (about 50 to about 500 microns).

20       26.      The stabilizing catheter of claim 1, wherein the protein drug is an insulin analogue.

25       27.      The stabilizing catheter of claim 26, wherein the insulin analogue is LISPRO.

20       28.      An infusion system for protein drug delivery to a user, the infusion system comprising:

      an infusion device housing;

25        at least one reservoir within the housing, wherein the reservoir is used for containing at least one protein for delivery to the user;

      a drive mechanism within the housing; and

      a stabilizing catheter having a distal end and a proximal end with the proximal end being

connected to the reservoir, wherein the stabilizing catheter includes at least one layer, the at least one layer including one or more materials that reduce diffusion of small molecules through the tubing to provide a stabilizing layer, such that when the stabilizing catheter is used to deliver at least one protein, the protein drug formulation is stabilized as compared with a protein drug 5 formulation delivered via a different tubing including one or more materials that are free of an effect that reduces diffusion of small molecules through the tubing.

29. The infusion system of claim 28, further including an exit tip connected to the distal end of the stabilizing catheter.

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30. The infusion system of claim 28, wherein the stabilized protein drug is maintained in the tubing to substantially prevent occlusions from being formed during delivery of the protein drug.

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31. The infusion system of claim 28, wherein the protein drug formulation is a high concentration insulin formulation.

32. The infusion system of claim 31, wherein the high concentration insulin formulation is greater than about 100U/ml.

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33. The infusion system of claim 28, wherein the insulin is an insulin analogue.

34. The infusion system of claim 33, wherein the insulin is LISPRO.

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35. The infusion system of claim 28, wherein the one or more materials of the at least one material layer includes materials selected from at least polytetrafluoroethane, saran (PVOC), glass, metal, derivatives of these materials, and mixtures of these materials.

36. The infusion system of claim 35, wherein the glass material includes glass fibers.

37. The infusion system of claim 35, wherein the metal material includes a braided metal.

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38. The infusion system of claim 28, wherein the stabilizing catheter includes more than one layer.

39. The infusion system of claim 35, wherein the stabilizing catheter further includes 10 a layer comprising a silicone material.

40. The infusion system of claim 39, wherein the layer comprising silicone is an outer layer of the stabilizing catheter.

15 41. The pump system of claim 40, further including an inner layer including materials selected from at least polytetrafluoroethane, saran (PVOC), glass, metal, derivatives of these materials, and mixtures of these materials.

42. The infusion system of claim 28, wherein the stabilizing catheter includes two 20 layers, an outer layer including a silicone and a layer including materials selected from at least polytetrafluoroethane, saran (PVOC), glass, metal, derivatives of these materials, and mixtures of these materials.

43. The infusion system of claim 28, wherein the one or more materials of the at least 25 one layer of the stabilizing catheter includes at least one elastomer.

44. The infusion system of claim 28, further including at least a second layer, wherein the second layer forms an innermost layer and is formed from one or more hydrophilic insulin compatible materials.

5 45. The infusion system of claim 28, wherein the insulin compatible materials are selected from at least a polyethylene glycol, a polyurethane, a Genapol, a Tween, a Triton and a Brig, derivatives of these materials and mixtures of these materials.

10 46. The infusion system of claim 28, wherein the small molecules have a molecular weight of about 18 g/mole to about 500 g/mole.

15 47. The infusion system of claim 28, wherein the small molecules include neutral molecules, charged molecules, or mixtures of these molecules.

20 48. The infusion system of claim 47, wherein the neutral molecules include at least phenol, phenolic derivatives, carbon dioxide, or mixtures of these molecules.

25 49. The infusion system of claim 47, wherein the charged molecules include metal ions.

50. The infusion system of claim 48, wherein the stabilizing catheter reduces a diffusional flow of carbon dioxide into the tubing by approximately 10-100 fold as compared to the diffusional flow of carbon dioxide into a different tubing that is free of a stabilizing layer.

51. The infusion system of claim 48, wherein the stabilizing catheter reduces a diffusional flow of phenol, phenolic derivatives, or mixtures of these molecules, out from the tubing by approximately 2-20 fold as compared to the diffusional flow of phenol, phenolic

derivatives, or mixtures of these molecules, out from a different tubing that is free of a stabilizing layer.

52. The infusion system of claim 28, wherein the stabilizing catheter provides a diffusional barrier to phenol, such that the loss of phenol through the tubing is less than about 5%, +/- 1%, at an insulin infusion rate of about 20 U/day.

53. The infusion system of claim 35, where the layer of Teflon and/or saran (PVOC) is about 0.002 in to about 0.02 in (about 50 to about 500 microns).

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54. A method of stabilizing a protein drug formulation in a drug delivery catheter, the method comprising:

15 providing a stabilizing catheter, wherein the stabilizing catheter includes at least one layer that includes one or more materials that reduce diffusion of small molecules through the tubing, such that when the stabilizing catheter is used to deliver the protein drug to a user, the protein drug is stabilized as compared with the protein drug delivered via a catheter that includes one or more materials that are free of an effect that reduces diffusion of small molecules through the catheter; and

20 flowing a fluid including the protein drug through the stabilizing catheter.

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55. The method of claim 54, wherein the stabilized protein drug is maintained in the tubing to substantially prevent occlusions from being formed during delivery of the protein drug.

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56. The method of claim 54, wherein the protein drug is a high concentration insulin formulation.

57. The method of claim 56, wherein the high concentration formulation is greater than about 100U/ml.

58. The method of claim 56, wherein the insulin is a human analogue insulin.

5 59. The method of claim 58, wherein the insulin is LISPRO.

60. The method of claim 54, wherein the one or more materials of the at least one layer includes materials selected from at least polytetrafluoroethane, saran (PVOC), glass, a metal, derivatives of these of these materials, and mixtures of these materials.

10 61. The method of claim 54, wherein the stabilizing catheter includes more than one layer.

15 62. The method of claim 54, wherein the stabilizing catheter comprises two layers, an outer layer including a silicone material and an inner layer including materials selected from at least polytetrafluoroethane, saran (PVOC), glass, a metal, derivatives of these materials, and mixtures of these materials.

20 63. The method of claim 54, wherein the small molecules have a molecular weight of about 18 g/mole to about 300 g/mole.

64. The method of claim 54, wherein the small molecules include neutral molecules, charged molecules, or mixtures of these molecules

25 65. The method of claim 54, wherein the neutral molecules include at least phenol, phenolic derivatives, carbon dioxide, or mixtures of these molecules.

66. The method of claim 54, wherein the charged molecules include metal ions.

67. The method of claim 54, wherein the stabilizing catheter maintains body fluids surrounding an implantable stabilizing catheter by reducing the diffusional flow of small molecules out from the stabilizing catheter and into a body of the user.

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68. A stabilizing catheter for protein drug delivery to a user, the stabilizing catheter comprising:

a tubing including at least one layer, wherein the at least one layer includes a stabilizing means that reduces the diffusion of small molecules through the stabilizing means, such that when the stabilizing means is used to deliver insulin, the protein drug formulation is stabilized as compared with the protein drug formulation delivered via a different tubing that includes one or more materials that are free of the effect that reduces diffusion of small molecules through the tubing.

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69. The method of claim 68, wherein the stabilized protein drug is maintained in the tubing to substantially prevent occlusions or deposits from being formed during delivery.

70. A stabilizing catheter for use in protein delivery to a site within the body comprising:

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a tubing including an interior surface; a hydrophilic and mobile layer that is in affixed to the interior surface of the tubing, wherein as the protein traverses through the tubing and is in contact with the hydrophilic and mobile layer, the protein substantially remains in its biologically/pharmacologically active form for delivery to a site within the body as compared to the same tubing that does not contain a hydrophilic and mobile layer on its interior surface.

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71. The stabilizing catheter of claim 70, wherein the protein is insulin.

72. The stabilizing catheter of claim 71, wherein the stabilizing substantially reduces site loss of insulin at the site of delivery within the body as compared to the same tubing that does not contain a hydrophilic and mobile layer on its interior surface.

5 73. A stabilizing catheter for use in protein delivery to a site within the body comprising:

a tubing that substantially reduces denaturation of the protein as it traverses through the tubing, thus maintaining the biologically/pharmacologically active form of the protein for delivery to the delivery site within the body.

10 74. A protein delivery tubing that maintains the biologically/pharmacologically active form of a protein drug for delivery to a delivery site within the body.

15 75. The protein delivery tubing of claim 74, wherein the delivery site is subcutaneous

76. The protein delivery tubing of claim 74, wherein the delivery site is intraperitoneal.

20 77. The protein delivery tubing of claim 74, wherein the protein drug is delivered via an external infusion drug delivery device

78. The protein delivery tubing of claim 74, wherein the protein drug is delivered via an internally implanted drug delivery device.

25 79. The protein delivery tubing of claim 74, wherein the delivery tubing includes a layer of a hydrophilic and mobile polymer affixed to the interior of the tubing.

80. The protein delivery tubing of claim 79, wherein the hydrophilic and mobile polymer includes polyethylene glycol.

81. A method of reducing site loss of a protein drug comprising:  
5 maintaining a biologically/pharmacologically active form of the protein drug for delivery to a site within the body via a catheter attached to a protein drug infusion device.

82 The method of claim 81, wherein the biologically/pharmacologically active form of the protein drug is maintained by controlling for changes in a protein drug formulation as it 10 traverses through the delivery catheter.

83. The method of claim 82, wherein the protein drug formulation is controlled for phenol and/or zinc loss.

84. The method of claim 81, wherein the resident time of the protein drug at a point 15 within the catheter is reduced by reducing the catheter diameter.

85. A method of reducing site loss of a protein drug comprising:  
providing a tubing with interior walls that form a surface;  
20 providing a hydrophilic and mobile coating the surfaces of the interior walls of the tubing;  
flowing a protein drug through the tubing to a desired site within the body; and  
delivering the protein drug to the desired site within the body in a biologically/pharmacologically active form.

86. The method of claim 85, further comprising providing a tubing that includes one 25 or more materials that substantially prevent the diffusion of small molecules into and out from the tubing.